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A REVIEW ON COMMON SECONDARY ANTECEDENTS OF RESISTANT HYPERTENSION AND ITS MANAGEMENT

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ABSTRACT

Hypertension is a state in which the force of the blood against the artery walls is too high usually 140/90, and is considered severe if the pressure is above 180/120. Hypertension becomes resistant due to uncontrolled blood pressure despite the use of three antihypertensive drugs, including a diuretic, in optimal doses. The most common antecedents or causes of resistant hypertensions are poor patient adherence, physician inertia, inadequate doses, excess alcohol intake, and incorrect combination of antihypertensive drugs. Patient whose blood pressure is controlled but require 4 or more medication to do so should also be considered resistant to the treatment. The secondary forms of resistant are endocrine disorders, renal disease, neurological disorders, chronic kidney disease, acute stress, drug induced hypertension, obstructive sleep apnea and primary aldosteronism. Most commonly it is found in the patients having chronic kidney disease and cardiovascular disease. The management of resistant hypertension includes the evaluation for secondary causes of hypertension, pharmacological management of resistant hypertension, newer drugs for the management of resistant hypertension, interventional management of resistant hypertension, reduction of dietary sodium intake, exclusion of drugs induced hypertension and verification of true resistant hypertension. This review mainly aimed at the common secondary antecedents of resistant hypertension and its management.

KEYWORDS: Resistant hypertension, obstructive sleep apnea, aldosteronism, secondary causes.

INTRODUCTION

Hypertension is a state in which the force of the blood against the artery walls is too high. Usually it is defined as above 140/90, and is considered severe if the pressure is above 180/120. Hypertension is one of the most common disease that represents a major public health problem affecting more than one billion people worldwide.[1] Resistant hypertension is currently defined as uncontrolled blood pressure including the use of optimal doses of three antihypertensive medications, of which major one is Diuretic.[2] The most common antecedents or causes of resistant hypertension are poor patient adherence, physician inertia, inadequate dose, inappropriate combination of antihypertensive drugs, and excess alcohol intake. Secondary forms of resistant hypertension includes endocrine disorders, renal disease, neurological disorders, acute stress, drug induced HTN,CKD,OSA, primary aldosteronism. These causes will contributes to the drug resistance to hypertension (2-10). The patients whose blood pressure is controlled but requires 4 or more medication to do so should be considered resistant to treatment. Resistant hypertension is not similar with uncontrolled HTN.

The list of causes of resistant hypertension are given below in (Table 1)

Causes of resistant hypertension (Table1)

1) Exogenous substances
* Drug related
* Herbal preparation
* Alcohol consumption
* Excess sodium intake

2) Concomitant condition
* Obesity
* Insulin resistance
* Smoking

3) Pseudo resistance
* White coat HTN
* Pseudo hypertension
* Physician inertia

4) Secondary causes of hypertension
* Renovascular disease
* Renal parenchymal disease
* Primary aldosteronism

* Pheochromocytoma
* Cushing's syndrome
* Thyroid and parathyroid disease
*Coarctation of the aorta

The real prevalence of resistant hypertension is unknown in the general population. For the effective management of patient with hypertension requires an effective combination of physiology and pharmacology, according to the characteristics of the patient. The management of resistant hypertension includes the evaluation for secondary causes of hypertension, pharmacological management of resistant hypertension, newer drugs for the management of resistant hypertension, reduction of dietary sodium intake, exclusion of drug induced hypertension and verification of true resistant hypertension. This paper mainly aimed at the common secondary antecedents of resistant hypertension and its managements.

OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea is the preserved and increased respiration effort despite partial or complete occlusion of the upper airway is a strong and independent risk factor for the presence and independent risk factor for the presence of HTN and cardiovascular diseases. The severity of OSA is related to various pathogenic mechanisms, that includes mainly hyperaldosteronism, increased, increased sympathetic tone, intermittent hypoxia and obesity.

Hyperaldosteronism: Hyperaldosteronism is a disease in which the adrenal gland make too much aldosterone which leads to hypertension (high blood pressure) & low blood potassium level. The excess production of aldosterone play an important pathophysiological role in relation between HTN and OSA.[3] Usually obese patients have higher level of aldosterone. As the obesity of the individual increases, that may lead to person to resistant hypertension. For example in the study of patients with resistant hypertension and control patients, the increased plasma aldosterone concentration and OSA were noted in patients with resistant hypertension but not in control subjects, show that excess may contribute to OSA severity.[4] All the studies pointing that hyperaldosteronism is an important factor that linking resistant hypertension and OSA.

Obesity: There is a linear correlation between obesity and OSA.In obese individuals, fat deposits in the upper respiratory tract narrow the airway, there is decrease in muscle activity in this region, leading to hypoxic and apneic episodes, ultimately resulting in sleep apnea. Studies shows that obstructive sleep apnea is believed to affect 25% of the adult population and as high as 45% of individuals with obesity. In adult individuals the most common cause of OSA is excess weight and obesity that is linked or associated with soft tissue present in the mouth and throat. At the time of sleeping, throat and tongue muscles are relaxed more, so this soft tissue can cause the airway to become blocked. Obesity, defined as BMI greater than or equal to 30, is the important risk factor for uncontrolled hypertension and OSA.[5,6,7,8] The factors which leads to obesity induced hypertension are impaired sodium excretion, increased sympathetic nervous system activity and the activation of renin angiotensin system.[4]

CHRONIC KIDNEY DISEASE AND RESISTANT HYPERTENSION

Hypertension is the state in which the force of the blood against the artery walls is too high. Hypertension is commonly found in patients with chronic kidney disease (CKD) with 75% of CKD patients taking antihypertensive drugs.[9] It is not only a common cause of resistant hypertension but also a consequence of poor blood pressure control over time. It is mainly affecting the renal system. Fluid retention, excessive activation of renin angiotensin aldosterone system and coincidental medicines are related to treatment resistance in patients with defective kidney function. Albuminuria and GFR should be noted in all patients with resistant hypertension. It is because the increase in serum creatinine occurs in the final stage of the disease, from the modification of diet in renal disease study can estimate the glomerular filtration rate.[10] Also the dietary salt reduction also having the role in reducing the volume expansion in chronic kidney disease. If any problem or block in the RAAS of patient having chronic kidney disease that will reduce the cardiovascular risk, improves BP control, and reduces proteinuria and progression to end stage renal disease.[11] Reductions in the glomerular filtration rate can after starting ACE inhibitor.

PRIMARY ALDOSTERONISM

Primary aldosteronism, indicate the over production of the hormone aldosterone from the adrenal glands, which leads to lower renin levels. This anomaly is caused by hyperplasia or tumors. The excess production of aldosterone leads to hypertension, metabolic alkalosis, hypernatremia, and potassium loss. Etc. which is finally considered as primary aldosteronism. It is usually occurs from an aldosterone producing adenoma, bilateral adrenal hyperplasia or rare familial syndromes. The prevalence of PA in the general hypertensive population remains an unresolved issue.[12,13] It is connected with hypertension. The prevalence of hypertension related to the severity of hypertension. In the study from Chile, PA was found in 1.99% of patients with stage 1 hypertension and in 13.2% of patients with stage 3 hypertension. All the data's shows that resistant hypertension represents the condition with the high chance of detecting PA.Is is find that both PA and OSA are coexisting in patients with resistant hypertension. In one study of 109 patients with resistant hypertension, OSA was found in 84% of patients with PA.In another study PA was found in only 34% of patients with OSA.[14] The endocrine related causes of secondary resistant hypertension are hypothyroidism, hyperthyroidism, acromegaly,

hyperparathyroidism, carcinoid tumor, congenital adrenal hyperplasia, and pheochromocytoma.

DRUG INDUCED HYPERTENSION

It is one of the major cause of secondary hypertension. The reason for the occurrence of drug induced hypertension is the variety of prescription and use of the over the counter medicine also the exogenous substance. Mainly two types of drug induced hypertension are there, one is NSAIDs induced hypertension and another one is oral contraceptives. Most common cause of drug induced hypertension is due to NSAIDs induced hypertension. Among them more than 50% is due to this NSAIDs. The NSAIDs makes the patient resistant. Data regarding the effect of NSAIDs on blood pressure continue to accrue. Consider two outlook cohort studies in normotensive woman reported high risk of following hypertension among NSAIDs users than in woman without regular NSAIDs intake.[15,16] The woman taking acetaminophen or NSAIDs will increase the risk two times for developing hypertension.[15] The use narcotic analgesic will also increase the risk for hypertension.[16] In the case of elderly hypertensive patients having osteoarthritis, indomethacin had no effect on blood pressure in patients who taking calcium antagonists but in the case of patients taking ACE inhibitors there is significant elevation of blood pressure.[17] Celecoxib exerted similar to placebo effects in patients taking ACE inhibitors it is a contrary.[18] Withdrawal of NSAIDs is indicated in patients having resistant hypertension, exacerbation of prior hypertension. Substituting NSAIDs with acetaminophen can usually relive the problem.

Oral contraceptives represents another very important cause of resistant hypertension.[19,20] Woman taking oral contraceptives had 80% higher risk of developing hypertension compared to woman not taking this kind of drugs. Withdrawal of this is high risk in those patients taking the drugs. Types of oral contraceptives also seems to be having clinical importance. The combined oral contraceptives like progestin and estradiol were widely used in the older days which associated with blood pressure elevation more frequently than progestin-only oral contraceptives.[21] All these shows that oral contraceptives may contribute to resistance in hypertensive women, but the type of oral contraceptive is important.

MANAGEMENT OF RESISTANT HYPERTENSION

Proper management of resistant hypertension is very important. It is a step by step approach involves, verification of true resistant hypertension, Exclusion of drug induced hypertension, Reduction of dietary sodium intake, Evaluation for secondary causes of hypertension, pharmacologic management of resistant hypertension, Newer drugs for the management of resistant hypertension, International management of resistant hypertension. Etc. The patient related problems can be assessed by treating with antihypertensive medication for the effective management of arterial hypertension. Physician related problems like physicians inertia contribute in treatment resistance. In order to achieve blood pressure goals doctors frequently reluctant to increase drug therapy by adding antihypertensive drugs.[22-25] The drug induced hypertension can be reduced by withdrawal of offended drugs usually results to the back of blood pressure to normal levels. By reducing the sodium intake in the food can reduce resistance. By evaluating the common secondary causes of resistant hypertension like obstructive sleep apnea, primary aldosteronism, chronic kidney disease...etc can reduce the hypertensive resistance. Mainly by reducing the obesity, snoring, daytime sleepiness, hypokalemia. Etc can reduce the chances of resistant hypertension. Most of the studies shows that spironolactone is a drug of choice for the treatment of resistant hypertension.[26-36] Chronotherapy indicate an important approach for the management of resistant hypertension. Administration of drugs of antihypertensive at bedtime has shown to improve blood pressure in resistant hypertensive patients.[37-39]

CONCLUSION

Resistant hypertension being a challenging clinical problem that is increasing day by day. Data from the clinical studies shows that major secondary antecedents of resistant hypertension are obstructive sleep apnea, primary aldosteronism, chronic kidney disease, drug induced hypertension and use of antihypertensive agents including diuretic. Data regarding the risk of resistant hypertension, as well as the benefits of treatment and control of blood pressure in resistant hypertensive patients is scarce. Data's shows that increased cardiovascular risk is present in patients with resistant hypertensio.Proper management of resistant hypertension is very important. It is a step by step approach involves, verification of true resistant hypertension, Exclusion of drug induced hypertension, Reduction of dietary sodium intake, Evaluation for secondary causes of hypertension, pharmacologic management of resistant hypertension, Newer drugs for the management of resistant hypertension, International management of resistant hypertension.

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